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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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2100 Pennsylvania Avenue NW
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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

253

DATE MAILED: 05/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No. 09/674,330	Applicant(s) HONJO ET AL.	
	Examiner Kathleen M Kerr	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 18 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 10-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 10-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s) _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a Final rejection (Paper No. 19, mailed on October 18, 2002), Applicants filed an amendment (previously not entered after-final) and a request for continued examination (RCE) received on March 18, 2003 (Paper Nos. 21 and 24). Said amendment amended Claims 1, 3, and 8. Thus, Claims 1-8 and 10-14 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the International Application No. PCT/JP99/02283 filed on April 28, 1999 and Japanese application 10-119731 filed on April 28, 1998.

Drawings

3. As previously noted, the drawings have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

Withdrawn - Objections to the Specification

4. Previous objection to the amendment filed July 25, 2002 (Paper No. 18) under 35 U.S.C. § 132 is withdrawn by virtue of Applicants' explanation of clear support in the specification as originally filed for the amendment.

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Withdrawn - Claim Rejections - 35 U.S.C. § 112

5. Previous rejection of Claims 1-8 and 10-14 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "having the same function" is withdrawn by virtue of Applicants' amendment.

6. Previous rejection of Claim 13 under 35 U.S.C. § 112, first paragraph, new matter, is withdrawn by virtue of Applicants' explanation of clear support in the specification as originally filed for the amendment.

7. Previous rejection of Claims 1, 3, 6-8, and 10-13 under 35 U.S.C. 112, first paragraph, written description, is withdrawn by virtue of Applicant's amendment inserting a functional limitation into the instant claims.

NEW OBJECTIONS/REJECTIONS

Claim Objections

8. Claim 3 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 depends from Claim 1; however, the subject matter of Claim 3 is not within the scope of that claimed in Claim 1. Thus, Claim 3 does not properly further limit the subject matter of the parent claim and must be rewritten in independent form.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-2 and 10-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "substantially" in Claim 1 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The Examiner suggests deleting the term "substantially" to obviate the instant rejection.
10. Claims 1-4, 6-8 and 10-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The inclusion of SEQ ID NOs: 3, 4, 8, or 9, and SEQ ID NOs: 1, 5, 6, or 10 is confusing due to the redundant sequences in the listing. The amino acid sequence of SEQ ID NO: 4 is equivalent to the amino acid sequence of SEQ ID NO:9; the DNA sequence of SEQ ID NO: 5 is equivalent to the DNA sequence of SEQ ID NO:10. Thus, the inclusion of redundant terms renders the claims indefinite.
11. Claims 1-3, 6-8 and 10-13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 1, the function of "functioning in the suppression of smooth muscle cell proliferation" is not particular and specific and lacks clarity. The Examiner

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suggests replacing this phrase with ---wherein said polypeptide suppresses smooth muscle cell proliferation--- in Claim 1 and similar language for Claims 3 and 8 for clarity.

12. Claim 12 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The abbreviation "PTCA" is unclear and must be defined upon its first appearance in the claims (see page 1 of the specification for a definition). Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 11-12 are rejected under 35 U.S.C. § 112, first paragraph, enablement, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To use the A55 polypeptide as a pharmaceutical composition for the treatment of specific conditions, such as abnormal smooth muscle cell growth and/or arteriosclerosis, would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as

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routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404).

Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

In the instant application, the activity of the mouse A55 polypeptide is tested using a BrdU assay and rat vascular smooth muscle cells (see Example 7); no test on the activity of A55b (the other isoform claimed) is performed, but the sequences are similar enough to extrapolate the same activity. While this data in combination with that of Nakamura *et al.* (see IDS #17) indicate **general** pharmaceutical applications, no suggestion of specific pharmaceutical applications is enabled. The Examiner notes that while the inventors are contributing authors of the Nakamura *et al.* publication, the data in the instant application supporting the function of the A55 polypeptide (Figure 1) is not included in said publication. Moreover, a different function of A55 (DANCE) is suggested by Nakamura *et al.* – that of a vascular ligand for integrin receptors in development and remodeling. Thus, to restate it, the use of the claimed pharmaceutical

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composition in general pharmaceutical applications is enabled considering the instant application and the art; however, the specific applications of the instant claims are enabled by neither the instant application nor the art.

No working examples or guidance for the pharmaceutical use of A55 polypeptides in the treatment of abnormal smooth muscle cell growth and/or arteriosclerosis is taught in the instant specification. The only experiments in support of the instant compositions must be extrapolated to support the claimed compositions from data not repeated in the published literature.

Additionally, the systems and pathways of abnormal cell growth and/or arteriosclerosis are highly complex. A particular pharmaceutical effect of the A55 protein is wholly unpredictable. Additionally, these experiments are in cultured cells; the nexus between cultured cells and *in vivo* results is highly limiting. The EGF-like domains could serve to interact with any one or more of the numerous EGF-like proteins in mammalian cells. One would then be required to assay for functionality, which assays are wholly unpredictable. The specification presents no guidance or working examples for such experimentation.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 3-5 and 14 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The instant claims, as written, do not sufficiently distinguish over cDNA as it naturally exists because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring

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products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified" as taught by the specification. See M.P.E.P. § 2105.

Summary of Pending Issues

15. The following is a summary of the issues pending in the instant application:
 - a) Claim 3 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.
 - b) Claims 1-2 and 10-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "substantially" which is a relative term.
 - c) Claims 1-4, 6-8 and 10-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the inclusion of SEQ ID NOs: 3, 4, 8, or 9, and SEQ ID NOs: 1, 5, 6, or 10 since some are redundant sequences.
 - d) Claims 1-3, 6-8 and 10-13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the function of "functioning in the suppression of smooth muscle cell proliferation".
 - e) Claim 12 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the abbreviation "PTCA".
 - f) Claims 11-12 are rejected under 35 U.S.C. § 112, first paragraph, enablement, as failing to comply with the enablement requirement.
 - g) Claims 3-5 and 14 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

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Conclusion

16. Claims 1-8 and 10-14 are rejected for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


KMK

May 27, 2003